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| APPLICATION NO.                                                                                                   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-------------------------------------------------------------------------------------------------------------------|-------------|----------------------|---------------------|------------------|
| 09/821,103                                                                                                        | 03/29/2001  | Robert Abramowitz    | TN17US(2548)        | 3256             |
| 23914                                                                                                             | 7590        | 10/20/2004           | EXAMINER            |                  |
| STEPHEN B. DAVIS<br>BRISTOL-MYERS SQUIBB COMPANY<br>PATENT DEPARTMENT<br>P O BOX 4000<br>PRINCETON, NJ 08543-4000 |             |                      | OWENS JR, HOWARD V  |                  |
|                                                                                                                   |             |                      | ART UNIT            | PAPER NUMBER     |
|                                                                                                                   |             |                      | 1623                |                  |
| DATE MAILED: 10/20/2004                                                                                           |             |                      |                     |                  |

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/821,103

**Applicant(s)**

ABRAMOWITZ ET AL.

**Examiner**

Howard V Owens

**Art Unit**

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 May 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                         |                                                                             |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                                |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____                                                             | 6) <input type="checkbox"/> Other: _____                                    |

### ***Response to Arguments***

The following is in response to the amendment filed 5/28/04:

An action on the merits of claims 1- 34 is contained herein below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### **Claim Rejections - 35 USC § 103**

Applicant's arguments filed have been fully considered but they are not persuasive. The rejection of claims 1-34 rejected under 35 U.S.C. § 103(a) as being unpatentable over Lin et al., U.S. Patent No. 4,978,655 and Ullah et al., U.S. Patent No. 6,607,747 is maintained for the reasons of record set forth below.

Applicant has provided evidence in this file showing that the invention was owned by, or subject to an obligation of assignment to, the same entity as 6,607,747 at the time this invention was made. Accordingly, 6,607,747 is disqualified as prior art through 35 U.S.C. 102(f) or (g) in any rejection under 35 U.S.C. 103(a) in this application. However, this applied art additionally qualifies as prior art under another subsection of 35 U.S.C. 102, 102(e) and accordingly is not disqualified as prior art under 35 U.S.C. 103(a).

Applicant may overcome the applied art either by a showing under 37 CFR 1.132 that the invention disclosed therein was derived from the invention of this application, and is therefore, not the invention "by another," or by antedating the applied art under 37 CFR 1.131.

Claim 1 is drawn to extruded-spheronized beadlets comprising stavudine, a spheronizing agent, and a quantity of magnesium stearate sufficient to stabilize stavudine against degradation during the extrusion-spheronization process.

Dependent claims 2-14 are drawn to modification of the beadlets with an antiadherent such as magnesium stearate, microcrystalline cellulose

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Claim 15 is the same as the composition set forth in claim 1; however, it contains a diluent. Dependent claims of 16-18 are drawn to the use of diluents such as corn starch, manitol and lactose. Dependent claim 19 is drawn to the use of a film former, polymeric barrier material and plasticizer.

Claims 21-30 are drawn to the compositions of either 1, 15 or 19 with an additional retroviral agent. Specifically didanosine in accordance with the species election of 11/03/2003.

Claims 31-34 are drawn to forming stavudine beadlets by formation of a wet mass of stavudine, extrusion and spheronizing the extrudate.

Lin teaches the formation of stavudine (d4T) in a composition with common pharmaceutical excipients –such as magnesium stearate, carboxymethyl cellulose and cellulose derivatives, diluents, protective matrices and polymeric substances for sustained delivery (col. 4, lines 10-43). Lin however does not specifically teach an extruded spheronized form nor the addition of didanosine. Ullah adequately bridges the nexus between Lin and the instant claims as it teaches the use of a pharmaceutical composition comprising an extruded spheronized (beadlet) containing the claimed plasticizers, coatings and carboxymethylcellulose binders for stability and modification of the dissolution profile (as well as beadlet formation) wherein the medicament may comprise didanosine or like acid labile compounds (col. 2., line 35 - col. 5, line 12; see also col. 5, line 55 – col. 6, line 16).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to form stavudine as a beadlet wherein various binders and excipients are used to add stability during processing and administration.

One of skill in the art would have been motivated to form stavudine as an extruded spheronized beadlet given that the prior art teaches that these spheronized beadlets allow for modification of the dissolution profile when administered and reduce the degradation of acid labile compounds, wherein didanosine and stavudine are exemplary of these compounds.


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As cited supra, since the Ullah reference is still prior art for the purposes of 103(a), the use of it to bridge the nexus for the teachings of Lin is also maintained. Applicant has not provided any response to the teachings of Ullah in combination with Lin.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Howard V. Owens  
Patent Examiner  
Art Unit 1623



James O. Wilson  
Supervisory Patent Examiner  
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538. The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.